COMMENTARY



A FAILED CANCER PARADIGM: implications for cancer risk assessment and patients

Edward J. Calabrese 1

Received: 25 June 2019 / Accepted: 27 June 2019 / Published online: 5 August 2019 © The International CCN Society 2019

Abstract

This commentary highlights the unique failures of environmental regulatory standards and related remedial actions to significantly reduce human cancer risks and the failure of cancer therapeutics to significantly impact cancer incidence and survival statistics despite vast resources allocated to both areas over the past half century. These dramatic institutional, scientific, medical, and regulatory failures suggest that current scientific understandings of cancer and its causation are seriously flawed and in need of a new objective re-appraisal.

Keywords Cancer · Precautionary principle · Dose response · Linear non-threshold · Hormesis · Risk assessment

Commentary

The role of the environment in cancer occurrence has been highly disputed over the past 50 years. In the 1970s, it was widely believed that environmental factors may account for up to 80% of human cancers. While this was initially thought to relate to the role of environmental contaminants, it became broadened to include diverse lifestyle factors, including diet, medicines and related factors. More recently, the role of environment in human cancer causation has been further questioned within the context of so-called "Bad Luck" mutations, which are claimed to account for some 70% of human cancers, thus greatly diminishing the belief in a dominant role of the environment in cancer causation, especially in the area of chronic low to very low dose exposures that are common in modern industrial societies. In fact, in the United States (US), substantial reductions in exposure to environmental carcinogens in the air, food and drinking water are generally not associated with decreased tumor incidence, with the exception

One Sentence Summary: Evidence is presented of a failed cancer paradigm that impacts both environmental regulation and cancer treatment therapies.

of smoking which should be seen as high dose carcinogen exposure.

A central issue is why cancer incidence and related deaths have not generally declined despite massive national and worldwide efforts to prevent assumed environmentally induced cancers and similar massive efforts to treat such affected individuals with research based therapeutic approaches. The striking failures to prevent the occurrence of cancer and a similar failure to markedly improve survival of cancer patients suggests that something is fundamentally wrong with the current accepted paradigms of cancer. This compels the reevaluation of not only our basic understanding of the biology of cancer but also the functional predictive utility of cellular and animal models in both a qualitative and quantitative sense. It also suggests that the biostatistical models that are used by regulatory agencies to estimate risks at low doses and upon which environmental standards are based may also provide highly unreliable information. Yet, environmental health beliefs and regulatory strategies are based on these approaches, typically without evidence of probing reflection by regulatory agencies and other leading groups that seem to be locked into dominating paradigms that have yielded profound scientific and clinical failure.

This situation calls for a top to bottom reappraisal of the "cancer problem". This challenge is central to society. Vast resources have been directed to prevent and cure this devastating disease, without the long hoped for successes. Despite the many collective worldwide trillions of dollars spent and vast research advances in many areas over a five decade



Edward J. Calabrese edwardc@schooolph.umass.edu

Department of Environmental Health Sciences; School of Public Health and Health Sciences; Morrill I, N344, University of Massachusetts, Amherst, MA 01003, USA

272 Calabrese EJ.

period the results are so strikingly anemic and so far off the mark to indicate that current fundamental understandings are seriously wrong and in need of a drastic rethinking and midcourse corrections.

As an initial step, there needs to be an objective and sober evaluation of the progress or lack thereof at multiple levels: theoretical, experimental, modeling and therapeutic. Many of these research areas do not typically communicate but there is a need for a genuine integrative new synthesis. In the late 1970s under the administrative and scientific leadership of Eula Bingham, the US Occupational Safety and Health Administration (OSHA) directed a national effort to develop a general scientific consensus to assess cancer risks from low doses of chemical and physical agents. Hundreds of experts testified with the information then synthesized and integrated, resulting in a massive publication in 1980. This effort was used by regulatory agencies to understand the cancer risk assessment issue and to formulate standard setting and create research and policy priorities. Now some 40 years later it is clear that far more needs to be done; society can not continue along the same path and expect a different and improved outcome. A new leadership effort should be initiated to address how societal efforts can lead to vastly improved understandings of the causation and successful treatment of cancer. The former US OSHA approach would be a good one to revisit as there needs to be a formal means by which governmental agencies such as US EPA and National Institutes of Health (NIH)/National Cancer Institute (NCI) can listen to scientific leaders in hopes of making the next 40 year period one in which it can deliver on the massive financial investments made to drastically reduce the incidence of cancer and make its clinical treatments far more successful.

Acknowledgements This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. EJC acknowledges longtime support from the US Air Force (AFOSR FA9550-13-1-0047) and ExxonMobil Foundation (S182000000000256). The views and conclusions contained herein are those of the author and should not be interpreted as necessarily representing policies or endorsement, either expressed or implied. Sponsors had no involvement in study design, collection, analysis, interpretation, writing and decision to and where to submit for publication consideration.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

